

CLAIMS

What is claimed is:

1. A WMI rat, wherein said rat exhibits a forced swim test immobility score of greater than about 9.
2. The WMI rat of claim 1, wherein said rat exhibits a forced swim test score of greater than about 11.
3. A WLI rat, wherein said rat exhibits a forced swim test immobility score of lower than about 8.
4. The WLI rat of claim 3, wherein said rat exhibits a forced swim test immobility score of lower than about 6.
5. A method of identifying a compound capable of treating a behavioral disorder in a mammal, said method comprising administering a test compound to a WMI rat, administering a placebo to an otherwise identical WMI rat, and assessing a behavior of each of said rats, wherein a change in said behavior of said rat administered said test compound, compared with the behavior of said rat administered said placebo, is an indication that said test compound is capable of treating a behavioral disorder in a mammal.
- 6 The method of claim 5, wherein said mammal is resistant to tricyclic and serotonergic antidepressants.
7. The method of claim 5, wherein said compound is a fast-acting compound.

8. The method of claim 5, wherein said behavioral disorder is alleviated.

9. The method of claim 5, wherein said behavior is assessed in a test selected from the group consisting of a forced swim test, an elevated plus maze test, a light/dark box test, an open field behavior test and a locomotor behavior test.

10. The method of claim 5, wherein said mammal is a human.

11. The method of claim 10, wherein said behavioral disorder is selected from the group consisting of major depression, bipolar depression, generalized anxiety disorder, obsessive compulsive disorder, post-traumatic stress disorder, dysthymia, cyclothymia and premenstrual syndrome.

12. A method of identifying a compound capable of treating a behavioral disorder in a mammal, said method comprising administering a test compound to a WLI rat, administering a placebo to an otherwise identical WLI rat, and assessing a behavior of each of said rats, wherein a change in said behavior of said rat administered said test compound, compared with the behavior of said rat administered said placebo, is an indication that said test compound is capable of treating a behavioral disorder in a mammal.

13. The method of claim 12, wherein said compound is a fast-acting compound.

14. The method of claim 12, wherein said mammal is resistant to tricyclic and serotonergic antidepressants.

15. The method of claim 12, wherein said behavioral disorder is alleviated.

16. The method of claim 12, wherein said behavior is assessed in a test selected from the group consisting of a forced swim test, an elevated plus maze test, a light/dark box test, an open field behavior test and a locomotor behavior test.

17. The method of claim 12, wherein said mammal is a human.

18. The method of claim 17, wherein said behavioral disorder is selected from the group consisting of major depression, bipolar depression, generalized anxiety disorder, obsessive compulsive disorder, post-traumatic stress disorder, dysthymia, cyclothymia and premenstrual syndrome.

19. A method of isolating a nucleic acid associated with a behavioral disorder in a mammal, said method comprising comparing mRNA obtained from a tissue in a WMI rat with mRNA obtained from the same tissue in a WLI rat and isolating nucleic acid corresponding to mRNA expressed in said WMI rat, which mRNA is either not expressed in said WLI rat or is expressed at a substantially lower level in said WLI rat, thereby isolating a nucleic acid associated with a behavioral disorder in said mammal.

20. The method of claim 19, wherein said mammal is resistant to tricyclic and serotonergic antidepressants.

21. The method of claim 19, wherein said comparison of said mRNAs is conducted by differential screening of libraries which are generated using said mRNAs.

22. The method of claim 21, wherein said comparison is conducted by suppressive, subtractive PCR.

23. The method of claim 19, wherein said comparison is conducted using reverse transcriptase PCR differential display.

24. The method of claim 19, wherein said tissue is selected from the group consisting of whole brain, amygdala, prefrontal cortex, hippocampus, and limbic brain region.

25. The method of claim 19, wherein said tissue is selected from the group consisting of amygdala, prefrontal cortex, and hippocampus.

26. A method of isolating a nucleic acid associated with a behavioral disorder in a mammal, said method comprising comparing mRNA obtained from a tissue in a WMI rat with mRNA obtained from the same tissue in a WLI rat and isolating nucleic acid corresponding to mRNA which is either not expressed in said WMI rat or which is expressed in said WMI rat at a substantially lower level than expression of said nucleic acid in said WLI rat, thereby isolating a nucleic acid associated with a behavioral disorder in said mammal.

27. The method of claim 26, wherein said mammal is resistant to tricyclic and serotonergic antidepressants.

28. The method of claim 26, wherein said comparison of said mRNAs is conducted by differential screening of libraries which are generated using said mRNAs.

29. The method of claim 27, wherein said comparison is conducted by suppressive, subtractive PCR.

30. The method of claim 26, wherein said comparison is conducted using reverse transcriptase PCR differential display.

31. The method of claim 26, wherein said tissue is selected from the group consisting of whole brain, amygdala, prefrontal cortex, hippocampus, and limbic brain region.

32. The method of claim 31, wherein said tissue is selected from the group consisting of amygdala, prefrontal cortex, and hippocampus.

33. A nucleic acid associated with a behavioral disorder in a mammal isolated by the method of claim 19.

34. An antisense nucleic acid which corresponds to the nucleic acid of claim 33.

35. A nucleic acid associated with a behavioral disorder in a mammal isolated by the method of claim 26.

36. An antisense nucleic acid which corresponds to the nucleic acid of claim 35.

37. A method of isolating a polypeptide associated with a behavioral disorder in a mammal, said method comprising comparing mRNA obtained from a tissue in a WMI rat with mRNA obtained from the same tissue in a WLI rat and isolating nucleic acid corresponding to mRNA expressed in said WMI rat, which mRNA is either not expressed in said WLI rat or is expressed at a substantially lower level in said WLI rat, thereby isolating a nucleic acid associated with a behavioral disorder in said mammal and obtaining the polypeptide encoded thereby.

38. The method of claim 37, wherein said mammal is resistant to tricyclic and serotonergic antidepressants.

39. The method of claim 37, wherein said comparison of said mRNAs is conducted by differential screening of libraries which are generated using said mRNAs.

40. The method of claim 39, wherein said comparison is conducted by suppressive, subtractive PCR.

41. The method of claim 37, wherein said comparison is conducted using reverse transcriptase PCR differential display.

42. The method of claim 37, wherein said tissue is selected from the group consisting of whole brain, amygdala, prefrontalcortex, hippocampus, and limbic brain region.

43. A polypeptide associated with a behavioral disorder in a mammal isolated by the method of claim 37.

44. An antibody which specifically binds to the polypeptide of claim 43.

45. A compound that modulates the activity of the polypeptide of claim 43.

46. A method of isolating a polypeptide associated with a behavioral disorder in a mammal, said method comprising comparing mRNA obtained from a tissue in a WMI rat with mRNA obtained from the same tissue in a WLI rat and isolating nucleic acid corresponding to mRNA which is either not expressed in said WMI rat or which is expressed in said WMI rat at a substantially lower level than expression of said nucleic acid in said WLI rat, thereby isolating a nucleic acid associated with a behavioral disorder in said mammal and obtaining the polypeptide encoded thereby.

47. The method of claim 46, wherein said mammal is resistant to tricyclic and serotonergic antidepressants.

48. The method of claim 46, wherein said comparison of said mRNAs is conducted by differential screening of libraries which are generated using said mRNAs.

49. The method of claim 48, wherein said comparison is conducted by suppressive, subtractive PCR.

50. The method of claim 46, wherein said comparison is conducted using reverse transcriptase PCR differential display.

51. The method of claim 46, wherein said tissue is selected from the group consisting of whole brain, amygdala, prefrontal cortex, hippocampus, and limbic brain region.

52. A polypeptide associated with a behavioral disorder in a mammal isolated by the method of claim 37.

53. An antibody which specifically binds to the polypeptide of claim 52.

54. A compound that modulates the activity of the polypeptide of claim 52.

55. An isolated cell obtained from a WMI rat.

56. An isolated cell obtained from a WLI rat.

57. A method of identifying a compound that regulates expression of a nucleotide sequence associated with depression or a behavioral disorder in a mammal, said method comprising contacting a cell from said mammal with said compound and determining whether the level of expression of said nucleotide sequence is altered in the presence of said compound compared with the level of expression of said nucleotide sequence in the absence of said compound, wherein a higher or lower level of expression in the presence of said compound is an indication that said compound regulates expression of said nucleotide sequence.

58. The method of claim 57, wherein said nucleotide sequence is selected from the group consisting of SEQ ID NOs:1-4.

59. A method of identifying a nucleic acid associated with depression or a behavioral disorder in a mammal, said method comprising isolating mRNA from a tissue in a WMI rat and isolating mRNA from the same tissue in a WLI rat, reverse transcribing said mRNAs to their respective cDNAs, performing subtractive suppressive PCR using the cDNA as both testers and drivers, and identifying those mRNAs exhibiting increased or decreased expression in tissue from WMI rats compared with tissue from WLI rats, thereby identifying said nucleic acid.

60. The method of claim 59, wherein said tissue is selected from the group consisting of whole brain, amygdala, prefrontal cortex, hippocampus, and limbic brain region.

61. The method of claim 60, wherein said tissue is selected from the group consisting of amygdala, prefrontal cortex, and hippocampus.

62. A nucleic acid associated with a behavioral disorder in a mammal isolated by the method of claim 59.

63. An antisense nucleic acid which corresponds to the nucleic acid of claim 62.

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